

# Aneurysmal subarachnoid hemorrhage affects the younger age groups in a Saudi academic center

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**BACKGROUND AND OBJECTIVES:** The epidemiology, clinical characteristics, and risk factors of aneurysmal subarachnoid hemorrhage (aSAH) in Saudi Arabia are still largely unknown. This retrospective cohort study was aimed to determine these features of the disease.

**DESIGN AND SETTINGS:** A retrospective cohort review was performed on all patients with aSAH who were treated and followed at King Abdulaziz University Hospital between July 2000 and December 2013.

**PATIENTS AND METHODS:** A quantitative methodology was used and data were collected on patients' age, gender, nationality, time to hospital presentation, clinical presentation, aneurysm characteristics, treatment, complications, and outcome.

**RESULTS:** A total of 41 patients with aSAH were included with a mean age of 43.2 (11.5) years; and males comprised 34.1%. Smoking and hypertension were the most common risk factors. Eight patients had known risk factors for aSAH, and were diagnosed using CT scans. An unfavorable outcome was associated with the presence of vasospasm ( $P < .001$ ), cerebral edema ( $P = .001$ ), and hydrocephalus ( $P = .003$ ).

**CONCLUSION:** A high occurrence of aSAH was observed in an age group younger than that reported in published reports. The pattern and outcome of aSAH were otherwise similar to prior reports. Future studies investigating these observations in other centers in the country can improve the prevention and treatment of this serious condition.

Subarachnoid hemorrhage (SAH) due to ruptured intracranial aneurysms represents 6% to 8% of all acute cerebrovascular diseases.<sup>1</sup> However, its importance is emphasized as it affects apparently healthy adults with often high risk of morbidity and mortality despite improvements in medical care. A significant proportion of deaths related to aneurysmal subarachnoid hemorrhage (aSAH) occurs even before patients reach the hospital or any specific treatment is considered.<sup>2</sup>

In Saudi Arabia, the incidence of aSAH is not known. Only a few retrospective studies were identified in published reports, collectively reporting on less than a 100 patients.<sup>3-5</sup> However, the importance of understanding the incidence, epidemiological and clinical characteristics, and risk factors for aSAH in Saudi Arabia cannot be overemphasized. It can eventually lead to improvements in prevention and treatment of this serious condition.

This epidemiological study aims to describe the characteristics and outcomes of patients with aSAH at a tertiary academic center in Jeddah.

## PATIENTS AND METHODS

A retrospective cohort review was performed using quantitative methodology. The medical records of all patients were reviewed with spontaneous SAH who were treated and followed up at King Abdulaziz University Hospital between July 2000 and December 2013. The Biomedical Ethics Research Committee of King Abdulaziz University granted permission to conduct the study.

### *Inclusion/exclusion criteria*

Patients were included provided they had a diagnosis of aSAH confirmed by computed tomographic (CT)

scan or cerebrospinal fluid examination, and a secular aneurysm was demonstrated on angiography (CT or digital subtraction catheter angiography). Cases excluded from the study were those were diagnosed with trauma, coagulopathy, or other non-aneurysmal vascular abnormalities like vascular malformation, vasculitis, or infective endocarditis. Furthermore, angiographically negative SAH and the cases transferred to other centers for endovascular treatment were excluded.

#### Clinical variables

Patients' demographics and presentation details were collected. Vascular risk factors and factors associated with aSAH were gathered including the history of hypertension, diabetes, and smoking. The World Federation of Neurological Surgeons (WFNS) clinical grading system was used to assess the symptoms' severity. In-hospital complications were also collected including the development of hydrocephalus, vasospasm, or cerebral edema. In-hospital outcomes were scored based on the Glasgow Outcome Score (GOS) and classified into unfavorable (GOS scores 1-3) or favorable (GOS scores of 4 or 5).

#### Statistical analysis

Descriptive statistics were performed for all variables, and expressed as frequency (percent) and as mean (standard deviation [SD]). The chi-square test was used to establish a relationship between categorical variables, and one-way analysis of variance was used to analyze continuous variables relative to multiple groups. Significance was set at  $P < .05$ .

## RESULTS

Of 77 patients with SAH, 50 patients were identified with angiographically detected aSAH. The other 27 patients had SAH secondary to trauma ( $n=16$ ), vasculitis ( $n=2$ ), cerebral vascular malformations ( $n=3$ ), mycotic/delochoectasia aneurysms ( $n=3$ ), or unknown etiology ( $n=3$ ) and were excluded. Nine patients with aSAH were excluded from this study because they were transferred within 48 hours to be treated at another center. The characteristics and outcomes of some of these patients were reported previously.<sup>6,7</sup>

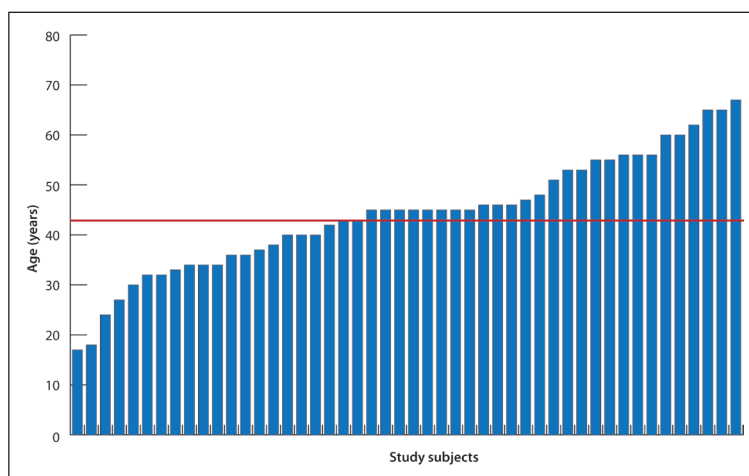
The included 41 patients had a mean (SD) age of 43.2 (11.5) years (range, 17-65 years). **Figure 1** shows the age distribution of the study sample. The mean (SD) and median (range) age for women were 43.4 (12.5) years and 43 (17- 67), respectively, while for men these were 45.7 (10.1) years and 46 (19- 60), respectively. Males comprised 34.1% ( $n=14$ ) of the sample,

and Saudis constituted less than the half (34.1%, **Table 1**). Two female patients were pregnant at the time of presentation. Twenty-seven (65.9%) of the sample were non-Saudis. The mean age at presentation in this group was 43.5 years, which was not different from the Saudi nationals (mean age 43.8 years).

The trend of annual admission of aSAH between 2000 and 2013 in our center is shown in (**Figure 2**). The mean time (SD) of presentation to hospital following the onset of symptoms was 2.6 (2.1) days (range, 1-10 days). The most common location of the identified aneurysms was in the anterior communicating artery region (36.6%, **Table 1**), and the mean aneurysm size (SD) was 11.4 (5.1) mm (range 5-27 mm). Over two-thirds of the patients ( $n=28$ , 68.3%) had no identifiable risk factors for aSAH, while 22% had a history of smoking or hypertension as risk factors (**Table 1**).

In most cases, ( $n=40$ ; 97.6%), there was evidence of SAH on brain CT scans. Seven patients had SAH-negative CT scans on admission 6 to 10 days after the symptoms' onset. However, the review of their initial reports revealed a positive SAH on the CT scan at the onset. One patient who had a negative CT scan for SAH at the onset had cerebrospinal fluid analysis documenting blood products.

A total of 36 (87.8%) patients were treated with microsurgical clipping, while 5 patients (12.2%) underwent endovascular coil occlusion of the aneurysms. The mean time from the symptoms' onset to treatment was 2.5 days. Regarding outcomes (**Table 2**), 29 patients (70.7%) had moderate to low disability; 15 patients (36.6%) had a GOS of 4, while 14 (34.1%) had a score of 5. Unfavorable outcome was associated with the development of vasospasm ( $P < .001$ ), cerebral edema

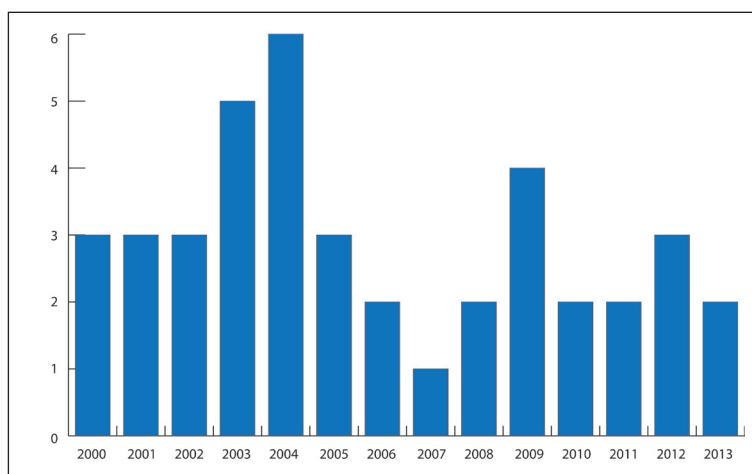


**Figure 1.** The age distribution of the subjects enrolled in this study. The red line points out the median age of the sample.

**Table 1.** Baseline clinical and imaging characteristics of the 41 patients with aSAH.

Characteristics		Frequency	Percent
Sex	Male	14	34.1
	Female	27	65.9
Nationality	Saudi	14	34.1
	Non-Saudi	27	65.9
SAH on CT scan	Yes	40	97.6
	No	1	2.4
Aneurysm location	Acom	15	36.6
	Basilar	1	2.4
	ICA	5	12.2
	ICA termination	2	2.4
	MCA	9	22
	Pcom	7	17.1
	R-PICA	1	2.4
	Pericallosal	1	2.4
WFNS grade	1	20	48.8
	2	8	19.5
	3	10	24.4
	4	3	7.3
Risk factors	None	29	70.7
	DM	3	7.3
	HPT	5	12.2
	Smoking	5	12.2

SAH: Subarachnoid hemorrhage; CT: computed tomography; WFNS: World Federation of Neurological Surgeons; ICA: internal carotid artery; MCA: middle cerebral artery; PICA: posterior inferior cerebellar artery; DM: diabetes mellitus; HPT: hypertension.



**Figure 2.** The number of cases of aneurysm subarachnoid hemorrhage (aSAH) during the study period.

( $P=.001$ ), or hydrocephalus ( $P=.003$ ). In-hospital outcome did not appear to be associated with patients' sex, presence of risk factors, evidence of SAH on brain CT, and treatment modality. Patients with WFNS grades 3 and 4 had significantly poorer outcomes compared to other WFNS grades ( $P=.001$ ).

## DISCUSSION

Published reports lack epidemiological data describing the incidence or characteristics of patients with aSAH in Saudi Arabia with only a few retrospective studies reported the characteristics of these patients. The report by Al-Mefty et al, in 1998, showed that only 24 cases of aSAH (among 54 cases of spontaneous SAH) occurred during a 10-year period at a tertiary medical center in Riyadh.<sup>3</sup> A study from a university hospital in Dammam by Ammar et al, in 1992, revealed only 29 cases of aSAH (among 73 cases of spontaneous SAH) occurred in 7.5 years.<sup>4</sup> The study by Jamjoom et al from a university hospital in Riyadh reported on 40 consecutive patients between 1984 and 1993.<sup>5</sup> These studies concluded that the incidence might be low compared to that observed in the rest of the world. In Jeddah city, where the estimated population was around 3 million and according to this single-institution study, an estimated occurrence of aSAH was calculated to be 2.5 cases per 100 000 (Figure 3).<sup>8</sup> These figures are expected to underestimate the true incidence given that patients in other public or in private hospitals are not captured. The lack of accurate figures for the catchment areas and the multiple health sectors are the likely explanation for the low volume of cases with aSHA reported in Saudi. Although at 1 point, it was believed that the incidence of aSAH is low in the Middle East and Saudi Arabia, researchers attributed these low numbers of aSAH cases to underreporting.<sup>3,9</sup> This stresses on the importance of acquiring better estimates through national multi-center study or cerebral aneurysm registries.

The mean age of patients in our study was 43.2 years, which is much lower than that reported in published reports. In a study by Zabihyan et al,<sup>10</sup> investigators reported a mean age of 50.3 years. In other hospital-based studies, the authors reported mean ages of 51 and 56 years for patients with aSAH.<sup>11</sup> Furthermore, prior population-based studies described that the incidence of SAH increases with age and is much less common before the age of 45 years,<sup>12</sup> with the estimated incidence in patients aged 35 to 45 years being half the incidence in those aged 45 to 55 years. The observation of young mean age of patients with aSAH could be explained by the small size and the selective nature of the sample in this study. However, the report by

Ammar et al also described in their sample a mean age of 29 and 21 years for males and females, respectively.<sup>4</sup> Similarly, the median age in the report by Jamjoom et al was 37 years.<sup>5</sup> If these observations are replicated in other studies, genetic vascular predisposition may be a factor unique to the patient population of this study that requires further investigation. This possible genetic predisposition is supported by the observation of lack of risk factors for cerebral aneurysm formation in over 70% of this study sample. However, the pathogenesis of saccular aneurysms is multifactorial.<sup>13</sup> Other new risk factors, including previous myocardial infarction, history of premature stroke in mother, and elevated cholesterol levels in men have also been associated with SAH.<sup>14</sup> Unfortunately, these risk factors were not assessed in the current study owing to the relatively small sample size.

The most common risk factors for aSAH in this study included smoking and hypertension, which have also been reported in patients with SAH.<sup>15</sup> However, the findings of this study demonstrate that only a low proportion of the patients had risk factors for aSAH. The relatively low frequency of smoking and hypertension in this study sample might be due to the small sample size, as recent studies reported increasing prevalence of smoking and hypertension in Saudi Arabia.<sup>16</sup> In another report, it was shown that smoking, hypertension, and excessive alcohol intake had significant and consistent associations with an increased risk of SAH in case-control and longitudinal studies.<sup>17</sup> In addition, the authors reported that the risk of SAH in former smokers was almost twice that of those who never smoked.

The other patients' characteristics and outcome in this study were similar to other reports in published reports. In this study, most ruptured aneurysms were located on the anterior communicating artery. This is consistent with prior local reports<sup>4</sup> although the study by Jamjoom et al described a slightly higher prevalence of anterior communicating artery aneurysms in their sample (50%). The patients with WFNS grades 3 and 4 in this study had unfavorable outcomes. While patients' sex did not affect the outcomes in this study, others reported that a male sex was associated with unfavorable outcomes.<sup>18</sup>

#### Limitations of the study

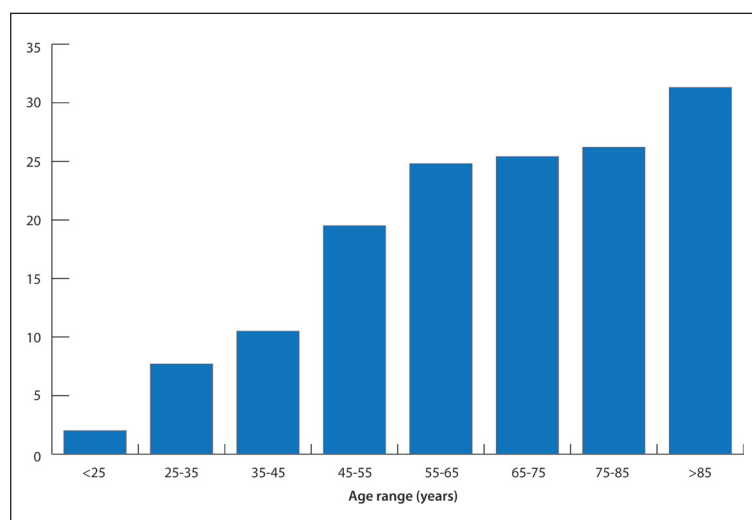
While this study is among the first in Saudi Arabia to describe the characteristics and outcome of aneurysmal SAH, it has some limitations because of the small sample and its retrospective nature. The limited sample size could be related to excluding patients with

non-aneurysmal SAH and those with mycotic aneurysms. All cases with unruptured aneurysms treated in the Saudi Academic center were also excluded. The nature of referral to this tertiary academic center may have played a role in limiting the volume of patients referred for intervention. Some of the factors sought were not documented in the patients' records, which included follow-up data for the discharged patients. Finally, as this was a single-center study, the generalizability of the results are limited.<sup>10</sup> Hence, future prospective multicenter studies should be performed to better assess the epidemiology of aneurysmal SAH in Saudi Arabia.

In conclusion, a high frequency of aSAH was ob-

**Table 2.** Treatment and outcome characteristics.

Variables		Frequency	Percent
Treatment modality	Microsurgical clipping	36	87.8
	Endovascular coiling	5	12.2
Vasospasm		16	39.0
Cerebral edema		12	29.3
Hydrocephalus		11	26.8
Glasgow outcome score	1	6	14.6
	2	1	2.4
	3	5	12.2
	4	15	36.6
	5	14	34.1



**Figure 3.** The estimated annual occurrence of aneurysmal SAH in the study of Jeddah based on this study.

served in the age groups younger than that reported in published reports. The pattern and outcome of aSAH were otherwise similar to published reports. Future studies investigating these observations in other centers in the country can improve the prevention and treatment of this serious condition.

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